

(54) PRODUCTION OF FREEZE-DRIED PRODUCT  
(11) 5-194194 (A) (43) 3.8.1993 (19) JP  
(21) Appl. No. 4-27170 (22) 17.1.1992  
(71) UNITIKA LTD (72) KOICHI UEMURA(2)  
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**PURPOSE:** To obtain a freeze-dried product causing no deactivation thereof, excellent in preservability and stability, thus useful as a food, medicine, etc., by packing a container with a solution containing one kind of physiologically active substance followed by freezing and then further packing the container with a solution containing another kind of physiologically active substance from above without the need of thawing and by repeating similar procedures for other physiologically active substance(s) followed by lyophilization.

**CONSTITUTION:** A container is first packed with a solution containing one kind of physiologically active substance (e.g. thrombin) followed by freezing, and then the container is further packed with a solution containing another kind of physiologically active substance (e.g. blood coagulating factor VIII) without the need of thawing the frozen product obtained in the preceding process; thence, such procedures are similarly repeated for other kind(s) of physiologically active substance(s), followed by lyophilization, thus obtaining the objective freeze-dried product.

(54) PRONANOSPHERE AND ITS PRODUCTION  
(11) 5-194196 (A) (43) 3.8.1993 (19) JP  
(21) Appl. No. 4-23367 (22) 14.1.1992  
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**PURPOSE:** To provide pronanospheres capable of producing nanospheres when redispersed in a solvent like water.

**CONSTITUTION:** Nanospheres containing a medicinal substance and phospholipid are, if needed, further incorporated with cholesterol, its derivative, or a substance capable of altering surface charge; the resulting nanospheres are applied on a sugaralcohol like sorbitol as nucleus by fluidized bed granulation process, thus obtaining the objective pronanospheres. Limitation of the weight ratio of the phospholipid to the medicinal substance can control the particle size of the nanospheres after their redispersion in water; furthermore, addition of the cholesterol can suppress particle size increase when the pronanospheres containing the medicinal substance at high concentration are redispersed in a salt-contg. aqueous solution.

(54) SUSTAINED RELEASE FINE PARTICLE PREPARATION COATED WITH ANTI-AGGREGATIVE AGENT  
(11) 5-194200 (A) (43) 3.8.1993 (19) JP  
(21) Appl. No. 4-262237 (22) 30.9.1992 (33) JP (31) 91p.253517 (32) 1.10.1991  
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**PURPOSE:** To provide a new polymeric fine particle preparation containing medicinal substance of uniform particle size with narrow particle size distribution, high in medicinal substance content, also low in the medicinal substance's initial releasing level.

**CONSTITUTION:** The objective polymeric fine particle preparation containing medicinal substance, coated with an anti-aggregative agent in a filmy fashion, can be obtained by subjecting (A) a medicinal substance-contg. polymer solution and (B) an aqueous solution of the anti-aggregative agent to spraying and mutual contact in a spray dryer using, respectively, separate nozzles.